

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C. 20231  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 07 June 2000 (07.06.00)	
<b>International application No.</b> PCT/US99/27452	<b>Applicant's or agent's file reference</b> 06510/056WO3
<b>International filing date</b> (day/month/year) 17 November 1999 (17.11.99)	<b>Priority date</b> (day/month/year) 25 November 1998 (25.11.98)
<b>Applicant</b> PRUSINER, Stanley, B.	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

25 April 2000 (25.04.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  Juan Cruz  Telephone No.: (41-22) 338.83.38
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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 09 MAR 2001

WIPO PCT

Applicant's or agent's file reference 06510/056WO3		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/27452	International filing date (day/month/year) 17/11/1999	Priority date (day/month/year) 25/11/1998	
International Patent Classification (IPC) or national classification and IPC G01N33/68			
Applicant THE REGENTS OF UNIVERSITY OF CALIFORNIA ET AL			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"><li>I <input checked="" type="checkbox"/> Basis of the report</li><li>II <input type="checkbox"/> Priority</li><li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li><li>IV <input checked="" type="checkbox"/> Lack of unity of invention</li><li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li><li>VI <input type="checkbox"/> Certain documents cited</li><li>VII <input checked="" type="checkbox"/> Certain defects in the international application</li><li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li></ul>			
Date of submission of the demand  25/04/2000		Date of completion of this report  06.03.2001	
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer  Giry, M  Telephone No. +49 89 2399 7328  	

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/27452

**I. Basis of the report**

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

**Description, pages:**

1-35 as originally filed

**Claims, No.:**

1-28 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/27452

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:  
**see separate sheet**

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-10, 17-19 and 20-28.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	1-10, 17-28
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10, 17-28
Industrial applicability (IA)	Yes:	Claims	1-10, 17-28
	No:	Claims	

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/27452

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2. Citations and explanations  
**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US99/27452

**Re Item IV**

**Lack of unity of invention**

The present application lacks the required unity-of-invention for the following reasons :

**Reference** is made to the following document :

D1 : US-A-5 792 901 (SCOTT MICHAEL R ET AL) 11 August 1998, cited in the application on p. 3, 5, 10, 23, 28 and 29 of the description.

The prior art document D1 discloses a standardized prion preparation, produced from harvested brain tissue from mammals which have their genome manipulated so that they are susceptible to infection with a prion which generally only infects a genetically diverse animal (col. 6, lines 1-10). Genetically diverse test animals may be human, cow or sheep (col. 6, line 60). Human polymorphisms, *e.g.* codon 129 Met/Val and pathogenic human mutations in the PrP gene, *e.g.* 2 octarepeat insert are also mentioned (col. 20, Mutation Table). The invention claimed in D1 also includes transgenic animals with their genome changed to include higher copy numbers of the PrP gene of the genetically diverse test animal (col. 19, lines 1-14). Prions produced in the transgenic mice Tg(HuPrP)/Prnp<sup>0/0</sup> and Tg(MHu2M) are also given as examples (col. 9, line 24 and 38, respectively).

Independent **claim 1** relates to a standardized prion preparation containing prions from a known strain present in a known amount and causing disease in a known species of animal. Independent **claim 11** concerns a prion protein standard composition containing isolated exogenous prions from transgenic mice together with a standard in brain homogenate from the animal that is normally infected with the prions used as a carrier.

The only technical features common to claims 1 and 11 is that they are prion protein standard compositions that contain prions and a carrier. However, document D1 discloses a standardized prion preparation with the same features. Therefore, claims 1-10 and 17-19 which are directed to the preparation of a prion standard according to claim 1 are not so linked to claims 11-16 as to form a single

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US99/27452

general inventive concept (Rule 13.1 PCT) as they appear not to be linked by a new special technical feature in the sense of Rule 13.2 PCT when taking into account the state of the art. Thus, the present application lacks unity of invention.

Therefore, two separate inventions are identified in the present application :

1 - Claims 1-10 and 17-19 :

A standardized prion preparation and methods of producing such preparations comprising prions and a carrier of a known composition which is **different** from brain tissue of the genetically diverse animal which the prions would infect in the animal's natural state, *e.g.* brain tissue of mice or water.

2 - Claims 11-16 :

A prion protein standard composition comprising prions and brain homogenate from the genetically diverse animal which the prions would normally infect.

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1 - **Reference** is made to the following document :

D1 : US-A-5 792 901 (SCOTT MICHAEL R ET AL) 11 August 1998, cited in the application on p. 3, 5, 10, 23, 28 and 29 of the description

2 - **Novelty** - Art. 33(1) and (2) PCT :

2.1 Claim 1 discloses a standardized prion preparation containing prions from a known strain present in a known amount and causing disease in a known species of animal. Since no standardized prion preparation characterized by a known amount of prions has already been described in the available prior art documents, claim 1 can be considered as new.

Claims 2-10 are dependent on claim 1 and as such also meet the requirements of the PCT with respect to novelty.

- 2.2 The method for preparing the prion protein standard disclosed in claim 17 is characterized by the inoculation of the host animals with a known amount of prions. For the reasons mentioned above (see point 2.1), claim 17 and 18-19 dependent thereon can therefore be considered as new.
- 2.3 Since none of the available prior art documents mention a calibration method for a prion assay, the subject-matter of claims 20-22 appears to be novel.
- 2.4 The same applies to the subject-matter of independent claim 23 concerning a prion protein standard kit and claims 24-28 dependent thereon.

**3 - Inventive step - Art. 33(1) and (3) PCT :**

- 3.1 As mentioned above (see Item IV), the closest prior art document D1 discloses methods for the detection of prions in a sample using a standardized prion preparation generated by transgenic mice methodology. In the light of D1, the problem underlying the present application is to be seen in providing alternative prion protein standard compositions and methods for calibrating prion protein assays. The invention also provides a prion protein standard kit comprising a plurality of protein preparations.
- 3.2 The subject-matter of claims 1 and 2 differs from document D1 by the known amount of prions present in the preparation. This distinguishing feature results in an improved accuracy of the standardized preparation. However, the skilled person who wishes to improve the assay reliability would regard it as a normal design procedure to include this feature in the prion preparation claimed in D1. Furthermore, the standardized prion preparation disclosed in document D1 also shares the technical features revealed in claims 3-10 (see Item V-1). Claims 1-10 can therefore not be regarded as inventive.



- 3.3 The subject-matter of claims 17-19 differs from D1 by the inoculation of the host animals with a known amount of prions, which is arbitrarily defined as a known number of infection units. As mentioned above (see point 3.2), this technical feature is considered an obvious option to improve the method for the preparation of a standard composition as claimed in D1. Thus, claims 17-19 do not appear to be inventive.
- 3.4 The method of calibration of a prion protein assay and the prion protein kit disclosed in the present application cannot be considered as inventive since they are characterized by technical features that fall within the scope of customary practice followed by person skilled in the art (e.g. determining a true value of protein concentration and accordingly adjusting the assay value ; the combinations of features as reported in claims 24-28). Thus, the subject-matter of claims 20-28 does not involve an inventive step.

**4 - Industrial applicability - Art. 33(1) and (4) PCT :**

The subject-matter of claims 1-10 and 17-28 appears to be industrially applicable.

**Re Item VII**

**Certain defects in the international application**

1. The expression "incorporated herein by reference" e.g. on p. 3 lines 3-4 of the description is not allowed as the application should be self-understanding (Art. 5 and Rule 9.1-iv PCT, see also PCT Guidelines III-4.3a).
2. The term "and the like" employed e.g. on p. 4 line 1 renders the description unclear (Art. 5 PCT, see also PCT Guidelines III-4.3a).
3. The vague and imprecise statement "scope of the invention" e.g. on p. 7 line 14 of the description implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity when

used to interpret them (Art. 6 PCT, see also PCT Guidelines III-4.3a). Such expressions are not allowed.

4. The paragraph corresponding to lines 22-26 on p. 7 of the description leads to confusion about the content of the application (Art. 5 and Rule 9.1-iv PCT).

**Re Item VIII**

**Certain observations on the international application**

1. According to the description (p. 4, lines 12-16), "the brain preparation is of a species genetically similar and more preferably the same as the species susceptible to infection". In contrast, claims 1 and 3 disclose a "carrier of a known composition which is different from brain tissue of the mammal which the prions would infect". The subject-matter of said claims therefore appears to be inconsistent with the description (Art. 6 PCT, see also PCT Guidelines III-4.3).
2. According to claim 1, the prions contained in the preparation are of a known strain. However, the subject-matter of the dependent claim 7 specifies that the prions are of different strains obtained from 10 or more animals. Claim 7 therefore appears to be inconsistent with the subject-matter of claim 1 (Art. 6 PCT, PCT Guidelines III-4.3).
3. The statement "known composition" in claim 1 is not clearly specified and renders the scope of the claim unclear (Art. 6 PCT).
4. The term "about" employed in claims 18 and 19 renders the said claims unclear (Art. 6 PCT, see also PCT Guidelines III-4.3a).

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Publication No

PCT/US 99/27452

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5792901 A	11-08-1998	US 5908969 A	01-06-1999
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		WO 9531466 A	23-11-1998



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Rec'd. 25 MAR 2002

Action by.....

Datum/Date

25.03.02

Zeichen/Ref./Réf. N.79174 DMG	Anmeldung Nr./Application No./Demande n°./Patent Nr./Patent No./Brevet n°. 98945791.6-2405-US9817879
Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire The Regents of the University of California	

## COMMUNICATION

The European Patent Office herewith transmits as an enclosure the European search report for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

## REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	US 5 565 186 A (PRUSINER STANLEY B ET AL) 15 October 1996 (1996-10-15) * column 3, line 54 - column 5, line 49 * * column 8, line 52 - line 55 * * column 14, line 31 - line 40 * ----	1-10	C12N15/00
X	WO 97 04814 A (UNIV CALIFORNIA) 13 February 1997 (1997-02-13) * page 11, line 4 - line 31 * * page 24, line 8 - page 29, line 29 * * page 45, line 11 - page 46, line 14 * ----	1-10	
X	BUSCHMANN A ET AL: "Generation of transgenic mice expressing the bovine prion protein (PrP)." JOURNAL OF MOLECULAR MEDICINE (BERLIN), vol. 75, no. 7, 1997, pages B176-B177, XP001061857 XIX Symposium of the International Association for Comparative Research on Leukemia and Related Diseases; Heidelberg, Germany; July 13-18, 1997 ISSN: 0946-2716 * the whole document * ----	1-10	
P,X	US 5 792 901 A (SCOTT MICHAEL R ET AL) 11 August 1998 (1998-08-11) * claims 1-12 * ----	1-10	
P,X	US 5 763 740 A (TELLING GLENN ET AL) 9 June 1998 (1998-06-09) * claims 1-13 * ----- -/-	1-10	
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
Place of search MUNICH		Date of completion of the search 7 March 2002	Examiner van Heusden, M
<div>CATEGORY OF CITED DOCUMENTS</div> <div><div>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</div><div>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- &amp; : member of the same patent family, corresponding document</div></div>			

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EPO FORM 1503 03.82 (Pa/C04)



DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
P,X	SCOTT MICHAEL R ET AL: "Identification of a prion protein epitope modulating transmission of bovine spongiform encephalopathy prions to transgenic mice" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 94, no. 26, 23 December 1997 (1997-12-23), pages 14279-14284, XP002158407 ISSN: 0027-8424 * the whole document *	1-10	
A	TELLING G C ET AL: "INTERACTIONS BETWEEN WILD-TYPE AND MUTANT PRION PROTEINS MODULATE NEURODEGENERATION IN TRANSGENIC MICE" GENES AND DEVELOPMENT, COLD SPRING HARBOR, NY, US, vol. 10, no. 14, 15 July 1996 (1996-07-15), pages 1736-1750, XP000675264 ISSN: 0890-9369 * the whole document *	1-10	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
A	PRUSINER S B: "Molecular biology and pathogenesis of prion diseases" TIBS TRENDS IN BIOCHEMICAL SCIENCES, ELSEVIER PUBLICATION, CAMBRIDGE, EN, vol. 21, no. 12, 1 December 1996 (1996-12-01), pages 482-487, XP004063036 ISSN: 0968-0004 * the whole document *	1-10	
-/--			
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
Place of search MUNICH		Date of completion of the search 7 March 2002	Examiner van Heusden, M
<b>CATEGORY OF CITED DOCUMENTS</b> X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

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EPO FORM 1503 03.82 (P04C04)



DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	GABIZON R ET AL: "Of mice and (mad) cows - transgenic mice help to understand prions" TRENDS IN GENETICS, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 13, no. 7, 1 July 1997 (1997-07-01), pages 264-269, XP004081447 ISSN: 0168-9525 * the whole document *	1-10	
T	PRUSINER STANLEY B: "Prions" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, no. 23, 10 November 1998 (1998-11-10), pages 13363-13383, XP002177728 ISSN: 0027-8424 * the whole document *	1-10	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
Place of search MUNICH		Date of completion of the search 7 March 2002	Examiner van Heusden, M
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2  
EPO FORM 1503 03.82 (P04C04)

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 98 94 5791

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on  
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07-03-2002

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EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82



**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 98 94 5791

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		NZ 284278 A	24-09-1998
		WO 9531466 A1	23-11-1995

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>06510/056W03</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/US 99/ 27452</b>	International filing date (day/month/year) <b>17/11/1999</b>	(Earliest) Priority Date (day/month/year) <b>25/11/1998</b>
Applicant  <b>THE REGENTS OF UNIVERSITY OF CALIFORNIA ET AL</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/US 99/27452

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/68 C07K14/47 G01N33/96

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 792 901 A (SCOTT MICHAEL R ET AL) 11 August 1998 (1998-08-11) cited in the application column 4, line 2-8,21-27 column 6, line 1-10,37-45 column 14, line 13-16,51-58 column 17, line 19-30 column 19 column 20 column 21, line 56-63	1-28
E	US 6 020 537 A (PRUSINER STANLEY B) 1 February 2000 (2000-02-01) the whole document	1-28
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

31 March 2000

Date of mailing of the international search report

25/04/2000

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/US 99/27452

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SCOTT M. ET AL.: "Propagation of prions with artificial properties in transgenic mice expressing chimeric PrP genes" CELL, vol. 73, 4 June 1993 (1993-06-04), pages 979-988, XP002133360 abstract	1-28
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